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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/820,975	04/07/2004	Daniel Santi	020547-003700US	9532

20350 7590 05/15/2007
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EXAMINER

POPA, ILEANA

ART UNIT	PAPER NUMBER
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1633

MAIL DATE	DELIVERY MODE
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05/15/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/820,975	Applicant(s) SANTI ET AL.	
	Examiner Ileana Popa	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 February 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-30 is/are pending in the application.
- 4a) Of the above claim(s) 21-30 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-20 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in the prior Office Action.
2. Claims 21-30 have been withdrawn. Claims 1 and 6 have been amended.
Claims 1-20 are under examination.

Response to Arguments

Double Patenting

2. The objection to claim 9 under 37 CFR 1.75 as being a substantial duplicate claim 8 is withdrawn in response to Applicant's arguments filed 02/08/2007.

Claim Rejections - 35 USC § 102

4. The rejection of claim 1 under 35 U.S.C. 102(b) as being anticipated by Siegal et al. (BioTechniques, 1996, 21, p. 614 and 617-619) is withdrawn in response to Applicant's amendment to the claim filed on 02/08/2007.
5. Claim 1 remains rejected under 35 U.S.C. 102(b) as being anticipated by Mandecki et al. (Gene, 1988, 68: 101-107) for the reasons of record set forth in the non-final Office action. Applicant's arguments filed 02/08/2007 (i.e., that there are three different vectors) have been fully considered but they are not persuasive.

Applicant traversed the instant rejection on the grounds that Mandecki et al. reference does not anticipate claim 1 because the reference describes a method entirely different from the instant invention. Specifically, Applicant argues that Mandecki et al. do not teach at least three different vectors and selecting a ligation product based on a selectable marker of one of the vectors. Therefore, Applicant requests the withdrawal of the rejection.

Applicant's arguments are acknowledged, however the rejection is maintained for the following reasons:

Mandecki et al. teach using four types of pUC-derived plasmid vectors (i.e., at least three different DNA vectors, each vector comprising *lacZ* as a selectable marker and each vector containing a DNA insert; after cleaving, the inserts are simultaneously ligated an cloned in pUC-derived plasmid comprising *lacZ* (i.e., selection of the ligation product is based on a selectable marker present on one of the DNA vectors) (p. 103, columns 1, first full paragraph and paragraph bridging column 2, column 2, first full paragraph, p. 104, column 1, p. 106, legend of Fig. 4). Mandecki et al. teach that their method is not limited to bridge mutagenesis (for example protruding ends can be generated) and that the method is applicable for applications such as gene assembly (p. 106 bridging p. 107). Therefore, Mandecki et al. teach all the claim limitations and the rejection is maintained (see also the non-final Office action).

5. The rejection of claims 1-6 and 18-20 under 35 U.S.C. 102(e) as being anticipated by Santi et al. (PGPUB 2004/0166567) is withdrawn in response to Applicant's arguments filed on 02/08/2007.

Claim Rejections - 35 USC § 103

6. Claims 1-20 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Lebedenko et al. (Nucleic Acids Research, 1991, 19: 6757-6761), in view of both Gokhale et al. (Science, 1999, 284: 482485) and Slater et al. (PGPUB 2005/0074883) for the reasons of record set forth in the non-final Office action. Applicant's arguments filed 02/08/2007 have been fully considered but they are not persuasive.

Applicant traversed the instant rejection on the grounds that the Examiner has failed to establish a *prima facie* case of obviousness. Applicant argues that Lebedenko et al. describe the cloning of a short DNA (about 500 bp in length) by a process involving multiple cycles of electrophoresis, elution, gel filtration, and *de novo* cloning, whereas a prototypical PKS-encoding sequence is over 30,000 bp in length. Therefore, one of skill in the art would have had no expectation of success in synthesizing a PKS gene (and therefore would not have had even a motivation to try) by using the method of Lebedenko et al. Regarding Gokhale et al., Applicant argues that the reference is entirely unrelated to the instant invention and it is cited only to show motivation to clone PKS genes. With respect to the limitation of DNA molecule each having a selectable marker and a counter selectable marker, Applicant argues that the Examiner fails to suggest any reason to modify the method of Lebedenko et al. to add a selectable and a

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counter selectable marker to the DNA fragments to be ligated or to the vectors carrying them. Applicant submits that it is not relevant whether the selectable and counter selectable markers were generally used in the prior art, because the claimed method was not known and it was not suggested by the cited references. With respect to the limitation of the presence of at least two Type 3 DNA molecules (claim 15), Applicant argues that the Examiner ignored the fact that Type 1, 2, and 3 DNA molecules each have different features and are used in combination in the claimed method (as described in the instant specification) and that the simple assertion that one of skill in the art would know to use more than one molecule does not provide a basis for an obviousness type rejection. Applicant also argues that the Examiner failed to suggest how and why the method of Lebedenko et al. would have been modified to use three DNA vectors as disclosed by the instant application. Therefore, Applicant requests the withdrawal of the rejection.

Applicant's arguments are acknowledged, however the rejection is maintained for the following reasons:

With respect to the argument that the Examiner failed to suggest how and why the method of Lebedenko et al. would have been modified to use three DNA vectors, it is noted that this limitation was not present in the original set of claims and it was introduced by the amendment to the claims filed on 02/08/2007 in response to the non-final Office action mailed on 04/19/2006. However, Lebedenko et al. teach this limitation. Specifically, Lebedenko et al. teach that the 3 DNA inserts containing the exons 5, 6, and 7 of the *IL-1 α* gene were cloned in three different pUC19 plasmids each

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comprising *lacZ* as a selectable marker (p. 6757, column 2 bridging p. 6758, p. 6758, column 1). Lebedenko et al. also teach their method as being suitable to assemble any gene, i.e., regardless of the length (p. 6760, column 2, second and third full paragraphs). Therefore, Applicant's argument that one of skill in the art would not have been motivated and would not have been expected to have a reasonable expectation of success in assembling larger gene is just an argument not supported by any evidence and it is not found persuasive. In response to Applicant's argument that Gokhale et al. is nonanalogous art, it has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). In this case, Gokhale et al. teach the modular structure of PKSs and the usefulness of recombining modules from the naturally-occurring PKSs by genetic manipulation (p. 482, column 2, p. 485, column 1). Therefore, Gokhale et al. provide a motivation for using the method of Lebedenko et al. to assemble PKS. With respect to the selectable and counter selectable markers, it is noted that the fact that they were well known and used in similar methods before the instant invention was made (see for example Slater et al., p. 2, paragraphs 0012 and 0013) is relevant because one of skill in the art would have known and motivated to use them in the method of Lebedenko et al. It is noted that Applicant's argument that Slater et al. was published after the filing of the instant application is not found persuasive because Slater et al. is applied under 102(e). Applicant argues that Type 1, 2, and 3 molecules, as disclosed by the instant

specification, each have different features and that they are used in combination in the claimed method and therefore the simple assertion that one of skill in the art would know to use more than one molecule does not provide a basis for an obviousness type rejection. This is not found persuasive because the specification discloses that the Type 1, 2, and 3 molecules differ only with respect to the selectable markers (see paragraph 0230) and this is not innovative over the prior art the prior because the prior art teaches the use of diverse selectable and counter-selectable markers and combinations thereof (see Slater et al., for example). One of skill in the art would know how to select markers to ensure that all inserts are present in the final product. Therefore, the instant method is rendered obvious by the teachings of the prior art and therefore, Applicant's argument that the claimed method was unknown is not found persuasive. For these reasons, the rejection is maintained.

Conclusion

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

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the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ileana Popa whose telephone number is 571-272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ileana Popa, PhD

Joe Woitach
AU 1633